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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference EX03-039C-PC	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US03/18262	International filing date (day/month/year) 11 June 2003 (11.06.2003)	Priority date (day/month/year) 12 June 2002 (12.06.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/495, 31/496, 31/5377; C07D 241/04, 401/06, 401/12, 403/06, 403/12, 413/06, 413/12. and US Cl.: 514/235.8, 252.11, 253.01, 253.05, 253.13, 254.01, 255.01; 544/121,357,360, 365, 372, 383.		
Applicant EXELIXIS, INC.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u> </u> sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>		
Date of submission of the demand 10 January 2004 (10.01.2004)	Date of completion of this report 23 August 2004 (23.08.2004)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Emily Bernhardt Telephone No. (571) 272-2717	

Form PCT/IPEA/409 (cover sheet)(July 1998)

I. Basis of the report**1. With regard to the elements of the international application:***

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-69 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the claims:
pages 70-93 as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 1-13, 15-27, 29-33, 35-40, 51-53, 64-66 (all in part)

because:

- ☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 1-13, 15-27, 29-33, 35-40, 51-53, 64-66 (all in part)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

Novelty (N)	Claims <u>4,5,14,17-28,34-50,54-63, 65-69</u>	YES
	Claims <u>1-3,6-13,15-16,29-33,51-53 and 64.</u>	NO
Inventive Step (IS)	Claims <u>4,5,14,17-28,34-50,54-63,65-69</u>	YES
	Claims <u>1-3,6-13,15-16,29-33,51-53 and 64.</u>	NO
Industrial Applicability (IA)	Claims <u>1-69</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-3,6-9,11-13,15,16,51-53 and 64 lack novelty and thus an inventive step under PCT Article 33(2)-(3) as being anticipated and rendered obvious by Bender (US'653). Bender describes many compounds within the instant scope having the same uses (eg. cancer, arthritis) as embraced by the method claims herein. See columns 4-6 and examples 1-9 in columns 25-35. Note that the final products in the examples are prepared employing sulfonyl halides of formula VIII.

Claims 1-3,10-12,15,16,29-33,51 and 53 lack novelty and thus an inventive step under PCT Article 33(2)-(3) as being anticipated and rendered obvious by Neya (US'324). Neya describes several compounds within the instant scope for uses such as cancer and arthritis. See columns 1,3 and 7 and examples 19,25,27-30 in columns 32,37 and 38.

Claims 4,5,14,17-28,34-50,54-63 and 65-69 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the structural makeup of piperazines claimed herein or starting materials in claims 65-69 or the multistep process embraced in claims 54-63.

Claims 1-69 meet the criteria set out in PCT Article 33(4), and thus possess industrial applicability because the subject matter claimed can be made or used in industry. A variety of pharmaceutical uses are described for piperazine final products claimed herein.